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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,710	10/03/2003	Arthur M. Krieg	C1039.70074US00	9983

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
08/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,710	KRIEG ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-47,52 and 94-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-47,52 and 94-100* is/are rejected.

7)☒ Claim(s) *46, 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/29/2008 has been entered.

Claim Objections

Applicant is advised that should claim 45 be found allowable, claim 52 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 45, 52, 95 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamamoto et al (1992) as evidenced by Tokunaga et al (1984, Abstract only).

Yamamoto et al disclose immunostimulatory sequences from known DNA which encode proteins of *Mycobacterium bovis* BCG (see whole document). In their previous work, the authors demonstrate that DNA extracted from BCG (MY-1) exhibit strong antitumor activity in mouse and guinea pig following intradermal injection (see Introduction, see Abstract only by Tokunaga). See Table 1 which provides specific sequences from BCG, including BCG-M2a (MPB70) and BCG-M5a (MPB70). Note that both of these sequences comprise one or more TCG motifs. The authors provide analysis of the augmentation of NK cell activity in Table II. The limitations of claims 45, 52, 95 and 100 have been met.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45, 47, 52, 95, 96, 97 and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al (1992) as evidenced by Tokunaga et al (1984, Abstract only) and Legendre and Szoka (1992).

The teachings of Yamamoto et al are applied as they are above (see 35 USC 102). This reference does not teach a using a cationic lipid as a DNA delivery complex.

Legendre and Szoka compare the delivery of DNA into mammalian cells using either pH-sensitive liposomes or cationic liposomes (Lipofectin) (see Abstract). The authors concluded that cationic liposomes mediate the highest transfection level in all cell lines examined (see Abstract and whole document). Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings above in order to deliver the BCG sequences provided by Yamamoto by way of the Lipofectin complex taught by Legendre and Szoka. One would have been motivated to do so given the successful results mediated by DNA/Lipofectin transfection described above. There would have been a reasonable expectation of success given both references provide successful results in either the antitumor effects by BCG DNA or efficient transfection using Lipofectin. Further, the underlying techniques are well described by the prior art and are widely known to one of ordinary skill in the art. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 45, 46, 47, 52, 94, 95, 98, 99 and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al (1992), (as evidenced by Tokunaga et al 1984, Abstract only) , Legendre and Szoka (1992) and US Patent No. 4824775 (hereinafter as "Dattagupta"), Boussiotis et al (1993) and Lagranderie et al (1993, Abstract only).

The teachings of Yamamoto et al and Legendre and Szoka are applied as they are above (see 35 USC 102 and 35 USC 103). These references do not teach administering an antigen (claim 46), cell targeting (claims 94, 95 and 98) and oral administration (claim 99).

Dattagupta teaches the attachment of either a specific protein or IgG for B-lymphocytes receptors to a DNA via a covalent reaction (see whole document and Figure 1 and Brief Summary). Boussiotis et al provides expression of three receptors identified by mAb (see Abstract). The identified CTLA-4 counterreceptors have been shown to costimulate T-cell proliferation (see whole document). The authors provide that these receptors may be responsible for the initiation and amplification of an immune response (see Discussion). Lastly, Langraderie et al describe the oral immunization with BCG-expressed foreign antigen (see claims 46 and 99 and Abstract). The authors demonstrate that the oral route of administration induced higher local and systemic immune responses than the intradermal route and that recombinant BCG can induce strong cellular and humoral immune responses.

Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings above in order to make a DNA/ cationic lipid complex further comprising a B

cell targeting peptide and an immunogenic antigen. One would have been motivated to do so in order to specifically stimulate B cells. Additionally, oral administration proved to induce greater immune responses compared to other routes while the BCG antigen induced strong immune responses (see Langraderie et al). There would have been a reasonable expectation of success because the underlying techniques are widely known and commonly used (see all references above). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45-47, 52 and 94-100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 63-66, 68 and 71-78 (withdrawn) of copending Application No. 10/928762. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same method steps for stimulating an immune response, including administering a composition comprising a CG motif via a lipid or a target cell specific binding agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-47, 52 and 94-100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42, 44-53, 59, 64-69, 71-73 and 75-80 of copending Application No. 10/719493. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same method steps for stimulating an immune response, including administering a composition comprising a CG motif and an antigen.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-47, 52 and 94-100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-52 of copending Application No. 11/071,836. Although the conflicting claims are not identical, they are not patentably distinct from each other because both

sets of claims are directed to the same method steps for stimulating an immune response, including administering a composition comprising a TCG motif.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-47, 52 and 94-100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42 and 44-48 of copending Application No. 11/503377. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same method steps for stimulating an immune response, including administering a composition comprising a TCG motif.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-47, 52 and 94-100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28, 29 and 31 of copending Application No. 11645106. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same method steps for stimulating an immune response, including administering a composition comprising a TCG motif.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648